Short Stature What is short stature? Short stature is a term used to describe a child who has not grown as tall as most other boys or girls their age. While short stature is somewhat subjective, it's typically defined as a person growing below the third percentile.

Anastrozole Increases Predicted Adult Height of Short Adolescent Males .

ORIGINAL ARTICLE

Endocrine Care

Anastrozole Increases Predicted Adult Height of Short Adolescent Males Treated with Growth Hormone: A Randomized, Placebo-Controlled, Multicenter Trial for One to Three Years

Nelly Mauras, Lilliam Gonzalez de Pjem, Helen Y. Hsiang, Paul Desrosiers, Robert Rapaport, I. David Schwartz, Karen Oerter Klein, Ravinder J. Singh, Anna Miyamoto, and Kim Bishop

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Context: The process of epiphyseal fusion during puberty is regulated by estrogen, even in males.

Objective: Our objective was to investigate whether anastrozole, a potent aromatase inhibitor, could delay bone age acceleration and increase predicted adult height in adolescent boys with GH deficiency.

Methods: Fifty-two adolescent males with GH deficiency treated with GH were randomized to cotreatment with anastrozole or placebo daily for up to 36 months.

Results: Fifty subjects completed 12 months, 41 completed 24 months, and 28 completed 36 months. Linear growth was comparable between groups; however, there was a significantly slower increase in bone age advancement from baseline in the anastrozole group *vs.* placebo group after 2 yr (+1.8 ± 0.1 *vs.* +2.7 ± 0.1 yr, $P < 0.0001$) and after 3 yr (+2.5 ± 0.2 *vs.* +4.1 ± 0.1 yr, $P < 0.0001$). This resulted in a net increase in predicted adult height of +4.5 ± 1.2 cm in the anastrozole group at 24 months and +6.7 ± 1.4 cm at 36 months as compared with a 1-cm gain at both time points in the placebo group. Estradiol and estrone concentrations increased less in the anastrozole group compared with placebo group. All boys on the aromatase inhibitor had normal tempo of virilization. Safety data, including glucose, and plasma lipid concentrations were comparable between groups.

Conclusions: Anastrozole increases adult height potential of adolescent boys on GH therapy while maintaining normal pubertal progression after 2–3 yr. This treatment offers an alternative in promoting growth in GH-deficient boys in puberty. Long-term follow up is needed to elucidate fully the safety and efficacy of this approach. (*J Clin Endocrinol Metab* 93: 823–831, 2008)

A number of strategies have evolved to increase height potential in GH-deficient children who are in puberty, such as using high-dose GH therapy (1) or GnRH analogs in addition to GH (2–5). The latter strategy has also been used in non-GH-deficient children, with mixed results (6–8). The consequences of gonadal suppression regarding bone accretion/bone density and the psychological impact of suppressing physiological puberty in an already short child have not been fully studied to date.

Studies of male patients with mutations in the estrogen receptor gene (9) or in the aromatase enzyme gene (10, 11) as well

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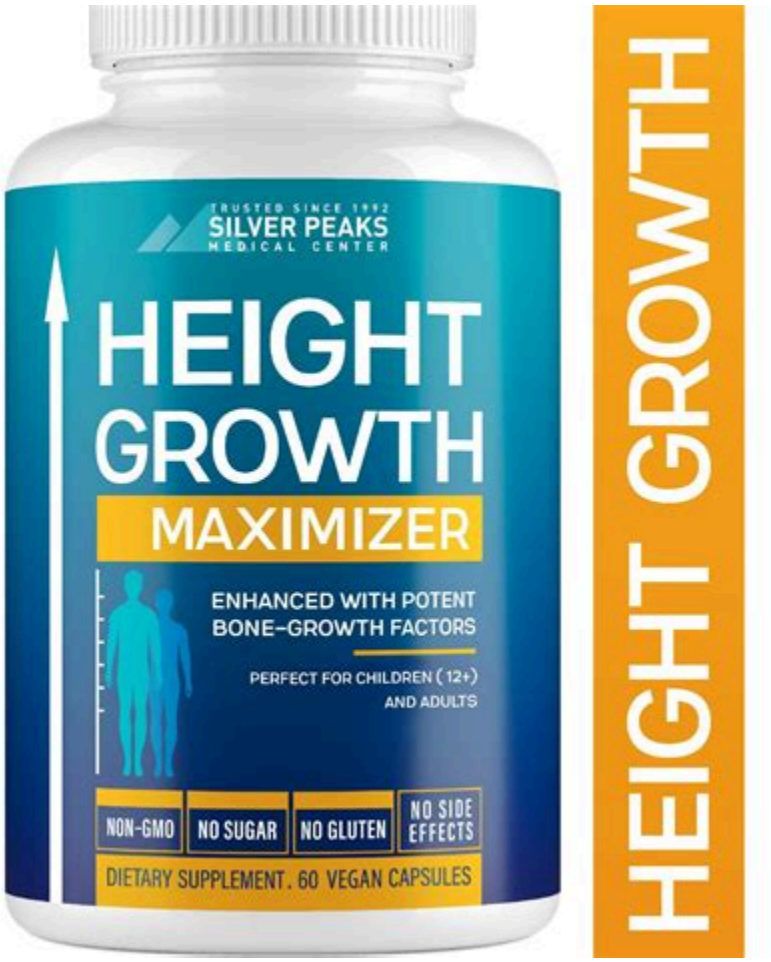
First Published Online December 28, 2007

Abbreviations: BMD, Bone mineral density; DXA, dual-energy x-ray absorptiometry; LC-MS/MS, liquid chromatography-tandem mass spectrometry; SDS, SD score.

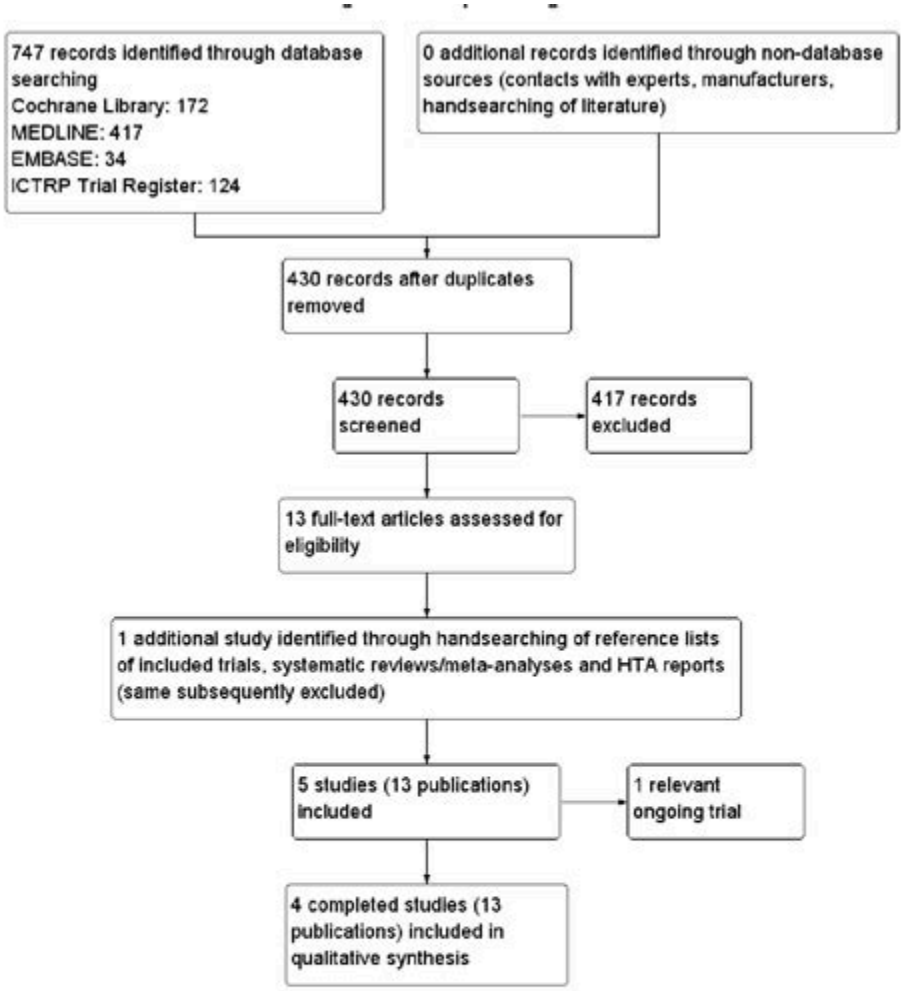
length gain, the width of the epiphyseal growth plates and GH levels. 46 Anastrozole administration to adult male rats had no effect on the number of Sertoli cells or germ cells, or on the volume of the seminiferous epithelium, tubule lumens or interstitium. 47 In female rats, exemes - tane increased weight gain and growth plate width, but

Increase Height And Grow Taller Using Letrozole And Anastrozole



Aromatase inhibitors (AIs) are a class of drugs that inhibit the aromatization step necessary for the formation of the estrogens. These drugs have been used in the treatment of breast cancer in postmenopausal women and gynecomastia in men [11, 12].

Aromatase inhibitors for short stature in male children and . - Cochrane



Aromatase inhibitors (AIs) have been used to recover height loss due to their capacity to delay growth plate closure. Long-term studies describing final heights are needed to determine the efficacy and safety profiles of these drugs for the treatment of impaired growth. This study aims to identify t …

Delayed closure of epiphyseal cartilages induced by the . - PubMed

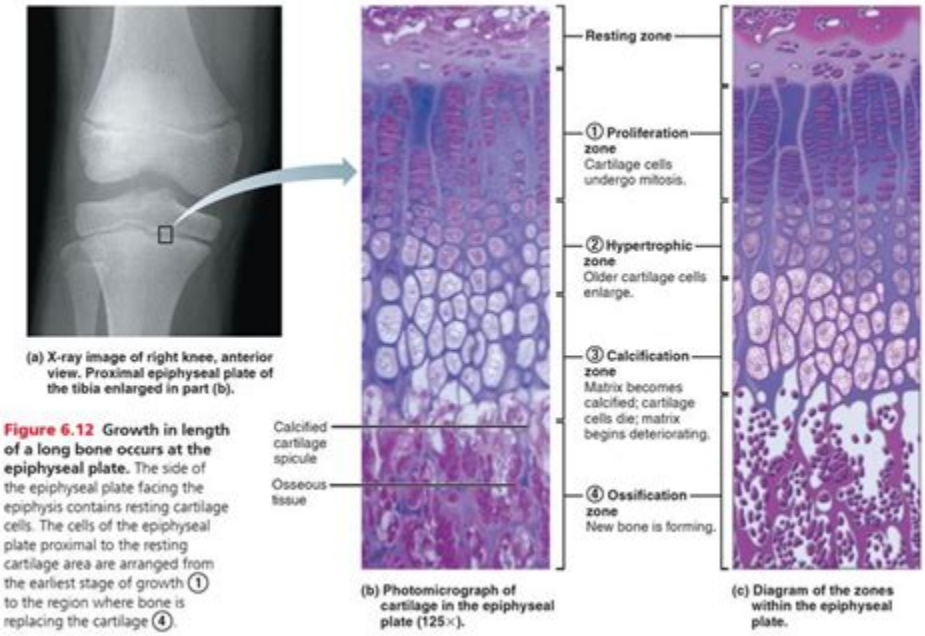


Figure 6.12 Growth in length of a long bone occurs at the epiphyseal plate. The side of the epiphyseal plate facing the epiphysis contains resting cartilage cells. The cells of the epiphyseal plate proximal to the resting cartilage area are arranged from the earliest stage of growth ① to the region where bone is replacing the cartilage ④.

Anastrozole side effects. Get emergency medical help if you have signs of an allergic reaction (hives, difficult breathing, swelling in your face or throat) or a severe skin reaction (fever, sore throat, burning eyes, skin pain, red or purple skin rash with blistering and peeling). . Anastrozole may decrease blood flow to your heart, especially if you have ever had coronary artery disease .

A randomized pilot trial of growth hormone with anastrozole versus .

Rothenbuhler et al. International Journal of Pediatric Endocrinology 2015, 2015:4
http://www.ijpeonline.com/content/2015/1/4

INTERNATIONAL JOURNAL OF PEDIATRIC ENDOCRINOLOGY

RESEARCH Open Access

A randomized pilot trial of growth hormone with anastrozole versus growth hormone alone, starting at the very end of puberty in adolescents with idiopathic short stature

Anya Rothenbuhler, Agnès Linglart and Pierre Bougnères*

Abstract

Background: When given during the course of puberty, anastrozole (A), an aromatase inhibitor, has been shown to increase the predicted adult height (PAH) of GH-deficient (GHD) boys treated with recombinant human growth hormone (rhGH). Our study questioned whether this treatment could retain some of its effects in non-GHD adolescent boys if started only at the very end of puberty, a time when rhGH treatment is denied to short adolescents who have almost reached their final height.

Objective: To explore the effect on adult height of a combination of rhGH and A, compared with rhGH alone, at the end of puberty in boys with idiopatic short stature (ISS).

Methods: A prospective randomized study comparing rhGH + A and rhGH was conducted in 24 healthy adolescent boys aged 15.2 ± 1.2 yrs with serum testosterone at adult levels and a faltering growth velocity <3.5 cm/yr leading to a predicted adult height (PAH) <2.5 SDS. Treatments were stopped when growth velocity became <10 mm in 6 months or when height was close to 170 cm. A historical group of ISS adolescents (N = 17) matched for puberty and growth was used for comparison.

Results: IGF1 levels remained within normal limits in all treated patients. Mean treatment duration was 19 months in the rhGH + A group and 11.5 months in the rhGH group ($P = 6.10^{-6}$). Adult height reached 168.4 ± 2.6 cm in the rhGH + A group and 164.2 ± 5.6 cm in the rhGH group ($P < 0.02$). Adult height was 160.1 ± 2.8 cm in the historical controls.

Conclusion: A combination of rhGH and A, started at the very end of puberty, seems to allow boys with ISS to reach a greater adult height than rhGH alone. Larger trials are needed to confirm this preliminary observation.

Keywords: Idiopathic short stature, Anastrozole, Growth hormone, Short children, End of puberty

Introduction

Idiopathic short stature (ISS) describes a heterogeneous group of children of unknown etiology [1-4] who become adults of short stature [5-18]. Based on general considerations on the tolerability of short stature by adults [19-30], and on the limited height benefit that is considered to result from years of a costly treatment whose long term safety has been questioned (see Discussion) [31-37], the use of recombinant human growth hormone (rhGH) to increase the height of healthy children with ISS remains debated. The prerequisites for the use of rhGH in ISS set by the FDA are that other diagnoses are excluded, that the presenting height is < −2.25 SDS for age and sex, and that adult stature is expected to be < −2.0 SDS [2]. Several reviews of studies on treatment with rhGH in ISS [1-3,38-40] concluded that a mean gain in predicted adult height (PAH) of ~5-7 cm can be expected following an average of 5.4 years of treatment. More meaningful information comes from studies that have provided adult height values [12-18,41-44]. In fact, the different studies showed different rhGH-induced height

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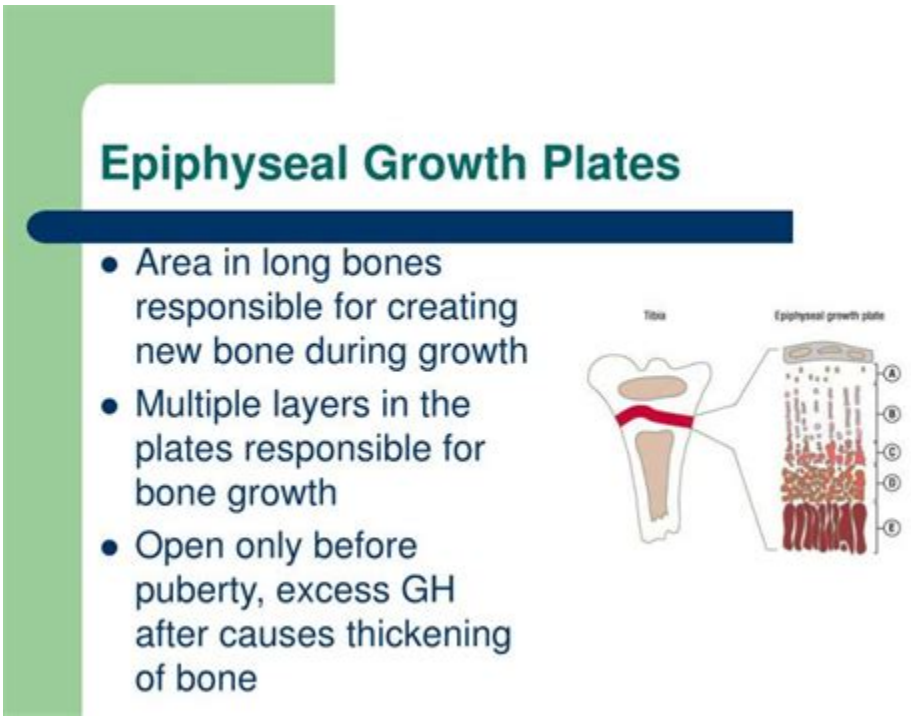
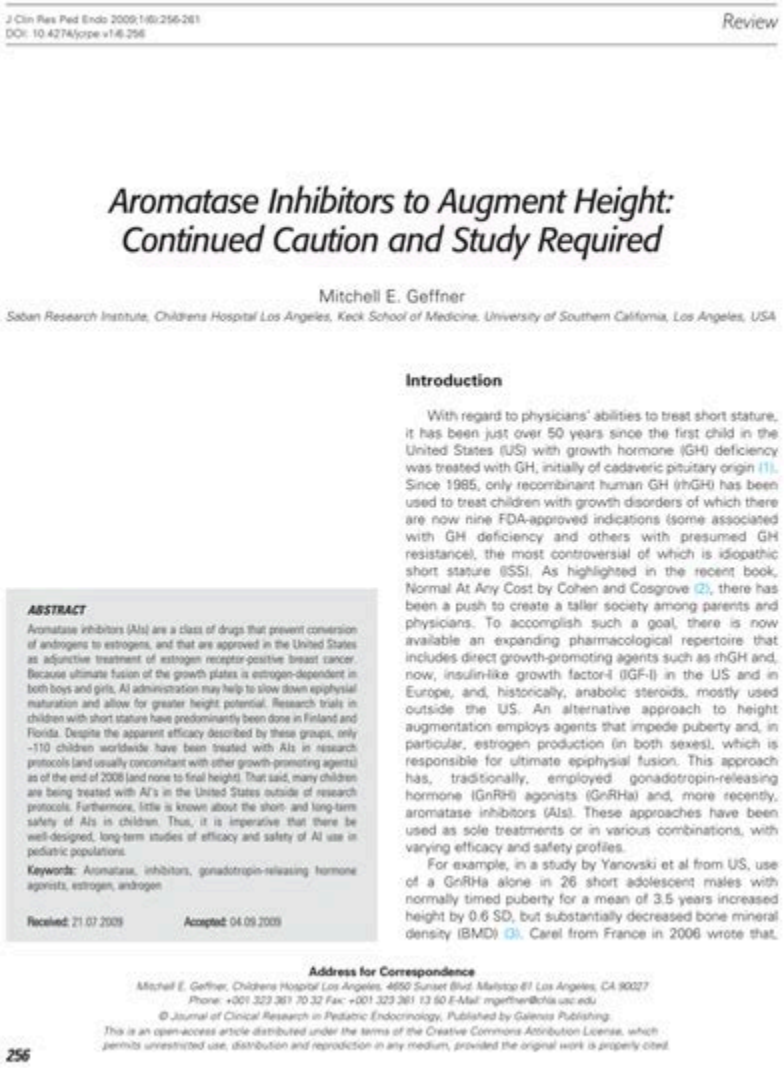
When given during the course of puberty, anastrozole (A), an aromatase inhibitor, has been shown to increase the predicted adult height (PAH) of GH-deficient (GHD) boys treated with recombinant human growth hormone (rhGH). Our study questioned whether this treatment could retain some of its effects in non-GHD adolescent boys if started only at the very end of puberty, a time when rhGH .

How to keep growth/ epiphyseal plates open - GTWSL



Would it help short children grow up? Delayed closure of epiphyseal cartilages induced by the aromatase inhibitor anastrozole. Would it help short children grow up? 2000 Dec;23 (11):721-3. doi: 10.1007/BF03345059. Aromatase Inhibitors* Bone Development / drug effects Growth Plate / drug effects* Nitriles / pharmacology* Nitriles / therapeutic use

Aromatase Inhibitors to Augment Height: Continued Caution and Study .



J Clin Res Ped Endo 2009;1(6):256-261
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Review

Aromatase Inhibitors to Augment Height: Continued Caution and Study Required

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Saban Research Institute, Childrens Hospital Los Angeles, Keck School of Medicine, University of Southern California, Los Angeles, USA

ABSTRACT

Aromatase inhibitors (AIs) are a class of drugs that prevent conversion of androgens to estrogens, and that are approved in the United States as adjunctive treatment of estrogen receptor-positive breast cancer. Because ultimate fusion of the growth plates is estrogen-dependent in both boys and girls, AI administration may help to slow down epiphysial maturation and allow for greater height potential. Research trials in children with short stature have predominantly been done in Finland and Florida. Despite the apparent efficacy described by these groups, only ~110 children worldwide have been treated with AIs in research protocols (and usually concomitant with other growth-promoting agents) as of the end of 2008 (and none to final height). That said, many children are being treated with AI's in the United States outside of research protocols. Furthermore, little is known about the short- and long-term safety of AIs in children. Thus, it is imperative that there be well-designed, long-term studies of efficacy and safety of AI use in pediatric populations.

Keywords: Aromatase, inhibitors, gonadotropin-releasing hormone agonists, estrogen, androgen

Received: 21.07.2009 **Accepted:** 04.09.2009

Introduction

With regard to physicians' abilities to treat short stature, it has been just over 50 years since the first child in the United States (US) with growth hormone (GH) deficiency was treated with GH, initially of cadaveric pituitary origin (1). Since 1985, only recombinant human GH (rhGH) has been used to treat children with growth disorders of which there are now nine FDA-approved indications (some associated with GH deficiency and others with presumed GH resistance), the most controversial of which is idiopathic short stature (ISS). As highlighted in the recent book, Normal At Any Cost by Cohen and Cosgrove (2), there has been a push to create a taller society among parents and physicians. To accomplish such a goal, there is now available an expanding pharmacological repertoire that includes direct growth-promoting agents such as rhGH and, now, insulin-like growth factor-I (IGF-I) in the US and in Europe, and, historically, anabolic steroids, mostly used outside the US. An alternative approach to height augmentation employs agents that impede puberty and, in particular, estrogen production (in both sexes), which is responsible for ultimate epiphysial fusion. This approach has, traditionally, employed gonadotropin-releasing hormone (GnRH) agonists (GnRHa) and, more recently, aromatase inhibitors (AIs). These approaches have been used as sole treatments or in various combinations, with varying efficacy and safety profiles.

For example, in a study by Yanovski et al from US, use of a GnRHa alone in 26 short adolescent males with normally timed puberty for a mean of 3.5 years increased height by 0.6 SD, but substantially decreased bone mineral density (BMD) (3). Carel from France in 2006 wrote that,

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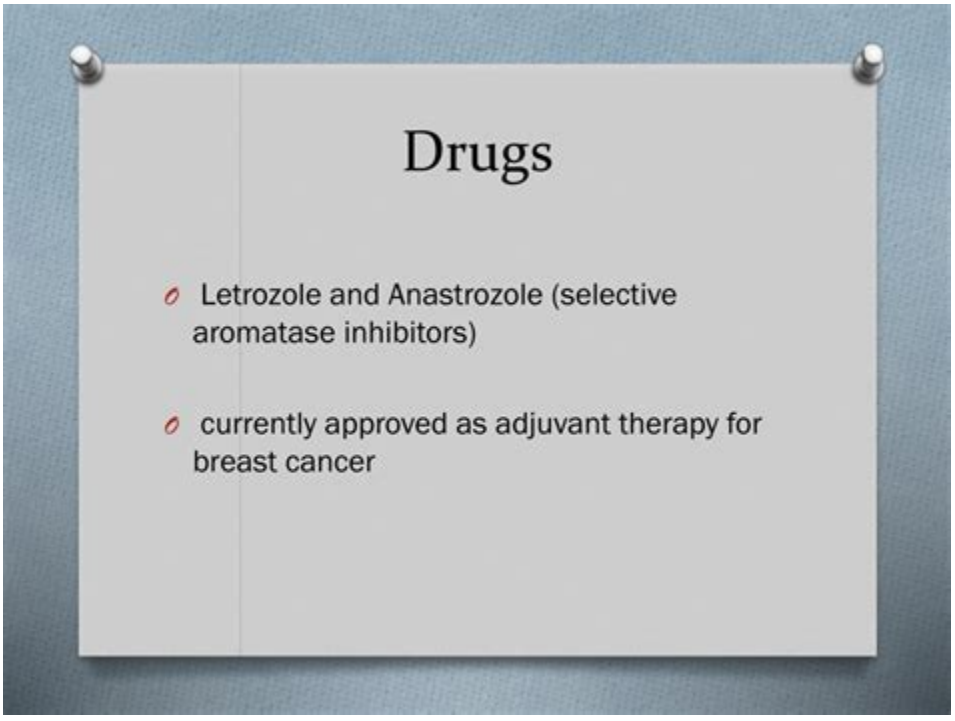
abnormal growth on your skin (lesion) open sores (ulcers) blisters. tickling, tingling, pain, coldness, or numbness in parts of your hand. Liver problems. Symptoms may include: yellowing of your .

Anastrozole Uses, Side Effects & Warnings - Drugs

Skeletal maturation can be delayed by reducing the exposure to estrogens, either by halting pubertal development through administering a GnRH analogue (GnRHa), or by blocking the conversion of androgens to estrogens through an aromatase inhibitor (AI). These agents have been investigated in children with growth disorders (off-label), either alone or in combination with recombinant human growth .

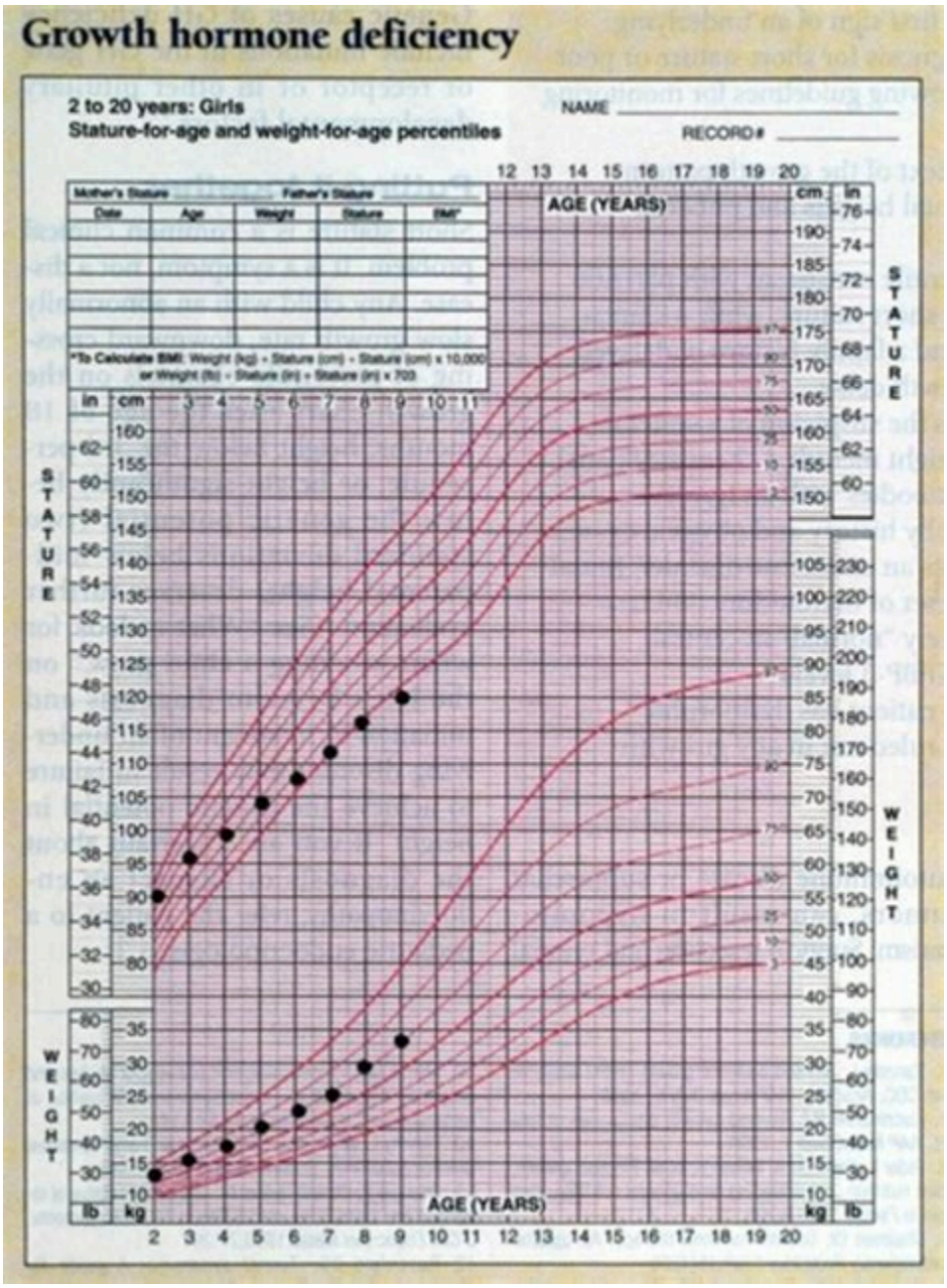
PDF Aromatase inhibitors in pediatrics - Stanford Medicine



Seventeen boys with constitutional delay of puberty were randomized to receive testosterone (T) enanthate (1 mg/kg i. m.) every 4 weeks for 6 months in combination with placebo (Pl, n = 8), or the aromatase inhibitor letrozole (Lz, 2. 5 mg/day orally) (n = 9), for 12 months. After treatment, patients

were followed up until near-final height.

Height outcomes in children with growth hormone deficiency and .



10. 1210/jc. 2007-1559 The process of epiphyseal fusion during puberty is regulated by estrogen, even in males. Our objective was to investigate whether anastrozole, a potent aromatase inhibitor, could delay bone age acceleration and increase predicted adult height in adolescent boys with GH deficiency.

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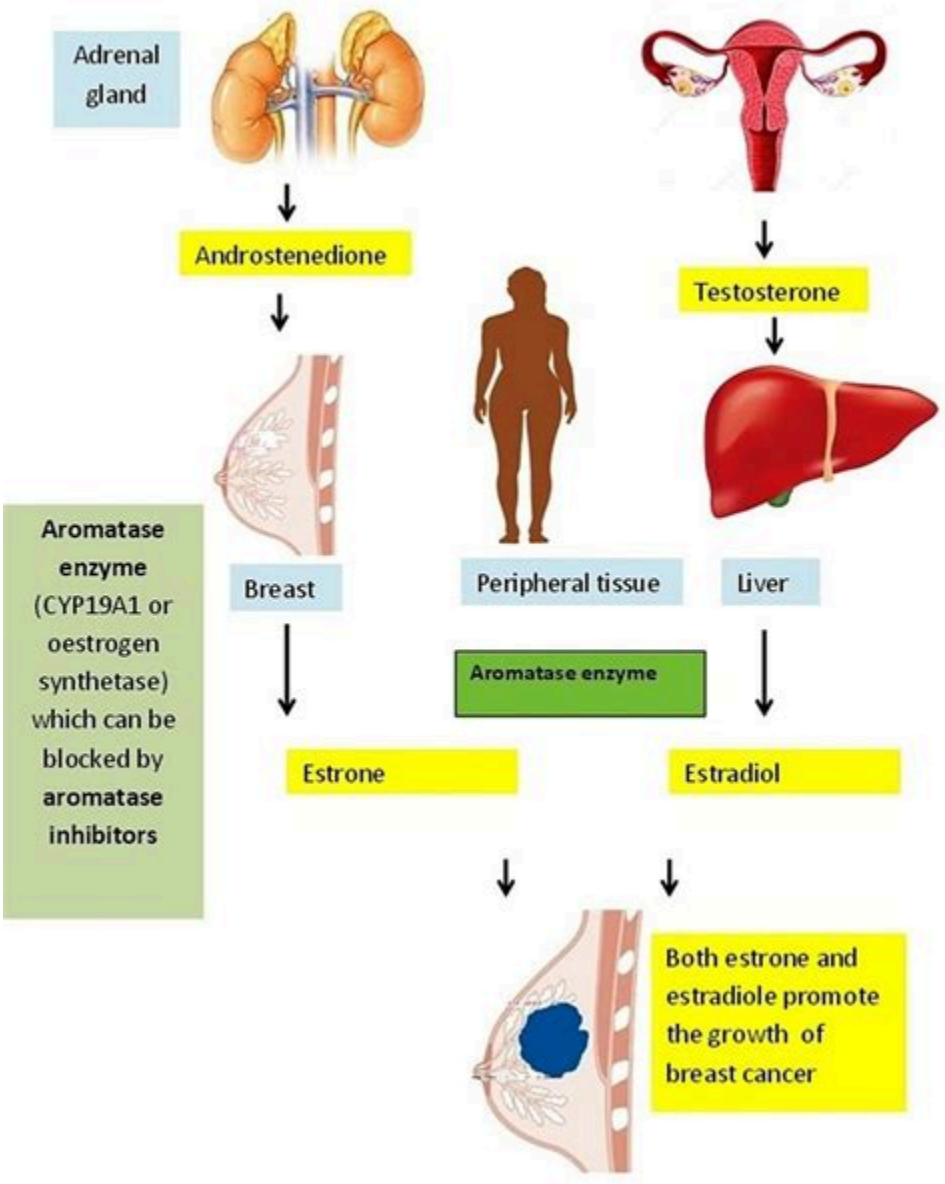
After 1. 5 years of anastrozole treatment, the patient's bone age advanced 6 months with robust linear growth. At chronological age 15 years 9 months, his bone age was 13 years 6 months, with height -1. 6 SDS and predicted adult height 178. 3 cm (+0. 2 SDS).

Aromatase inhibitors plus growth hormone may help short . - ScienceDaily

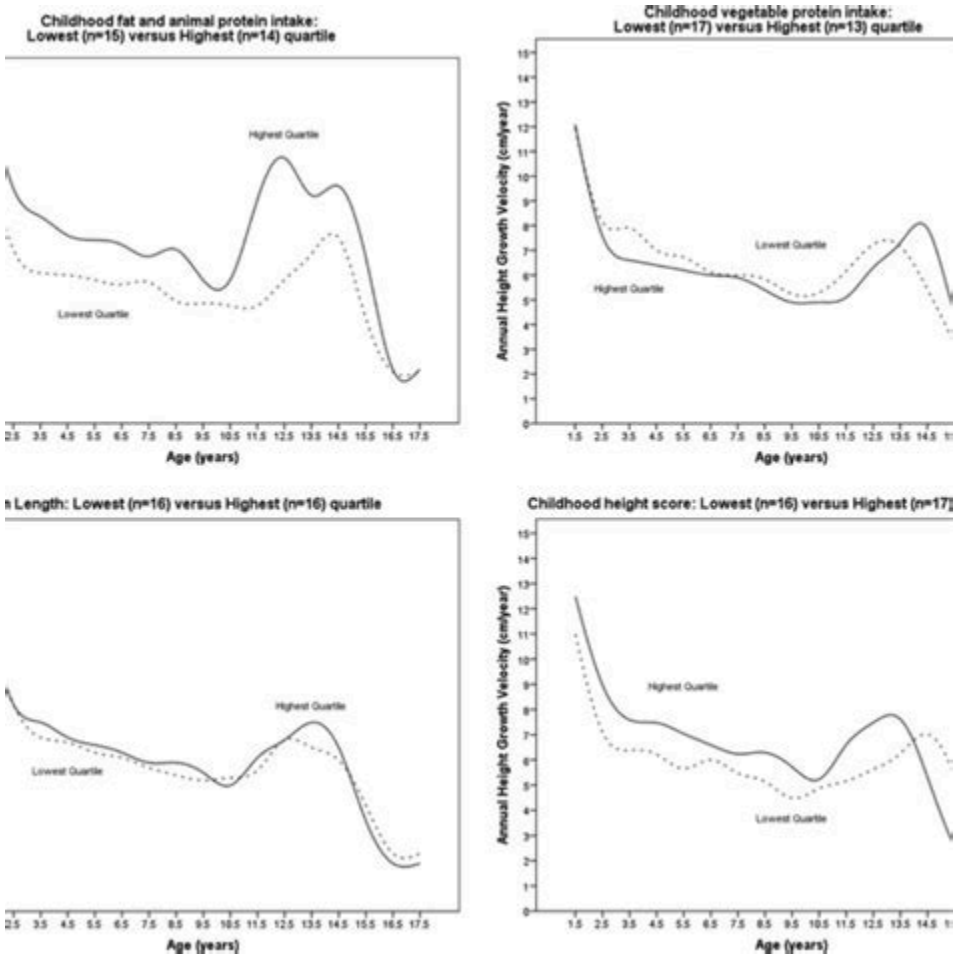


Abstract. Context: The process of epiphyseal fusion during puberty is regulated by estrogen, even in males. Objective: Our objective was to investigate whether anastrozole, a potent aromatase inhibitor, could delay bone age acceleration and increase predicted adult height in adolescent boys with GH deficiency. Methods: Fifty-two adolescent males with GH deficiency treated with GH were .

Anastrozole: Side Effects, Dosage, Uses and More - Healthline

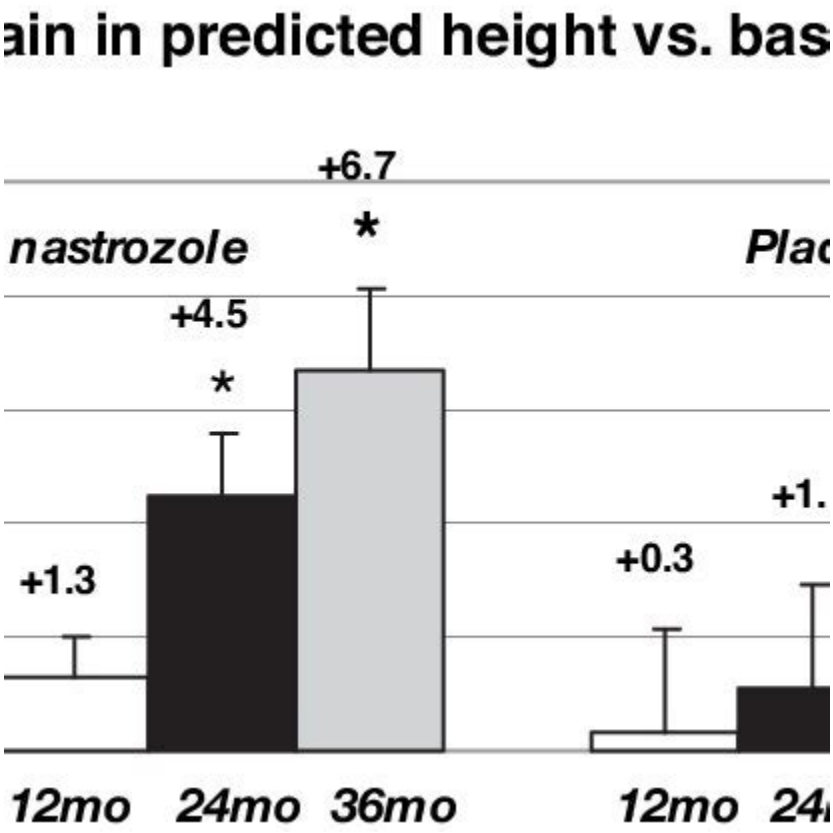
How to check if Growth Plates are still open X- ray scans can be taken for bones under investigation to check if growth plates are still open at home or hospital. X - ray showing Open and Closed plates. How Growth takes place at the Epiphyseal Plate. In brief, skeletal growth at the epiphyseal plate is active and constantly changing.

Height Increment and Laboratory Profile of Boys Treated With . - PubMed



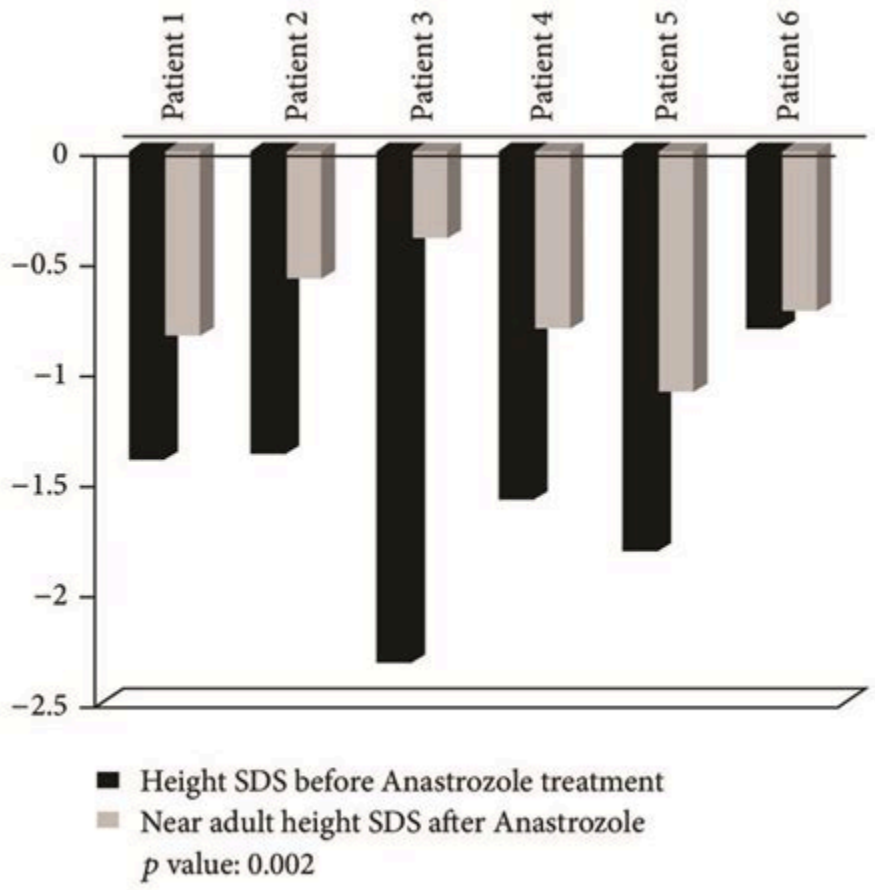
Accepted 26 Apr 2017 Published 22 May 2017 Abstract Background. Data on adult height outcomes of the use of Anastrozole and Growth Hormone (GH) in pubertal males with Growth hormone deficiency (GHD) and Idiopathic short stature (ISS) are limited. Objective.

Anastrozole increases predicted adult height of short . - PubMed



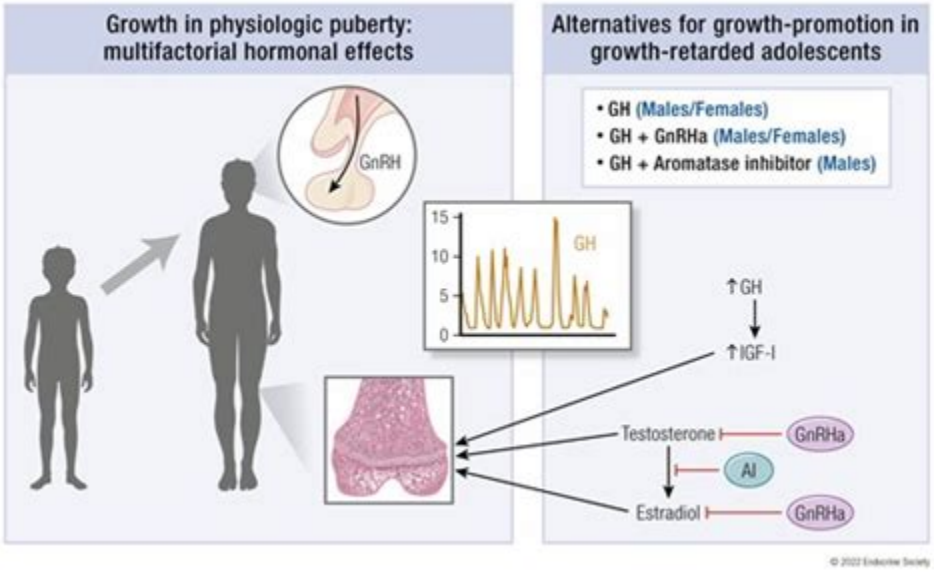
Available evidence suggested that aromatase inhibitors improved short-term growth outcomes. There was no evidence to support an increase in final adult height, based on limited data, with only one of four trials publishing final height data under non-randomised conditions. Read the full abstract. Health topics:

Anastrozole Improves Final Adult Height in Severe Hypothyroidism With .



Clinical experience with using an aromatase inhibitor to suppress estrogen production during puberty for improvement of growth potential in adolescents with short stature is limited. This report documents treatment of such a patient with a combination of growth hormone and letrozole, a third-generation aromatase inhibitor. Our case demonstrates a favorable outcome on a short-term basis.

Aromatase inhibitors in puberty - ScienceDirect

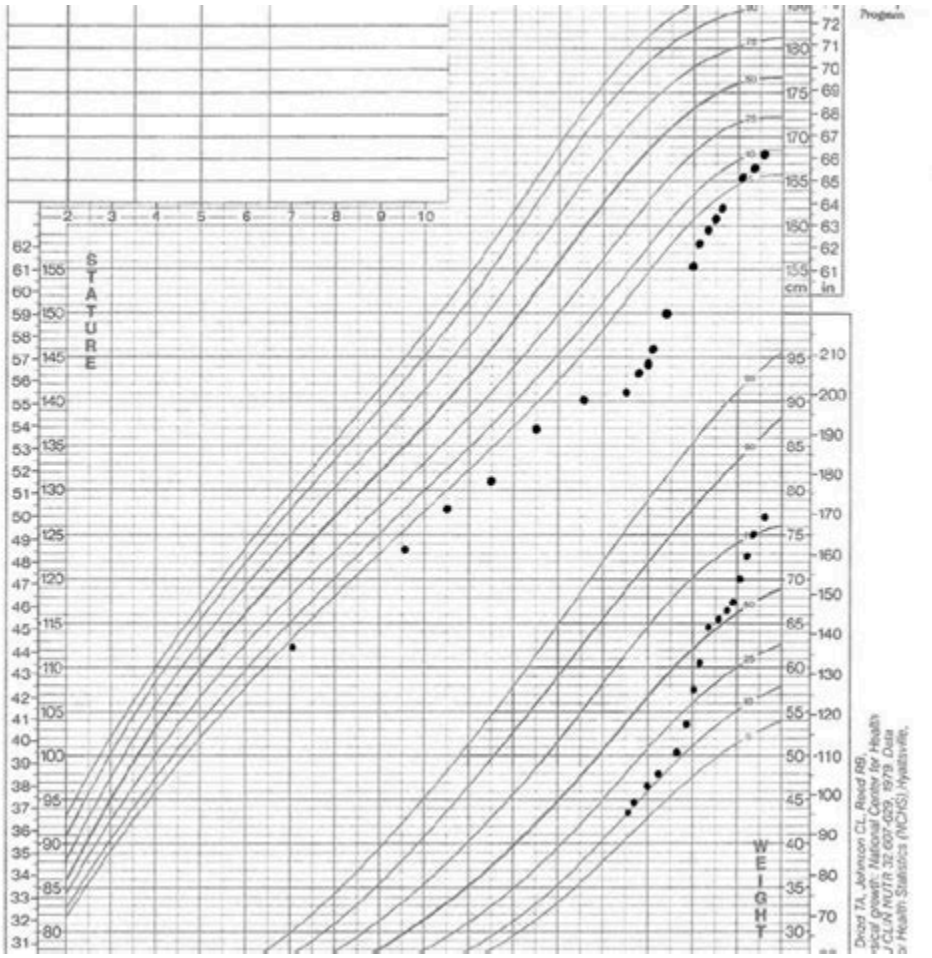


An observational study investigated whether recombinant GH (0. 076 mg/kg*d) and anastrozole could increase height in sexually mature adolescents with ISS (baseline mean age, 15. 2 years; BA, 14. 5 years) who had almost reached their adult height but had yet to experience complete growth plate fusion. Both GH and GH plus anastrozole increased final .

Short Stature | Children's Mercy Kansas City

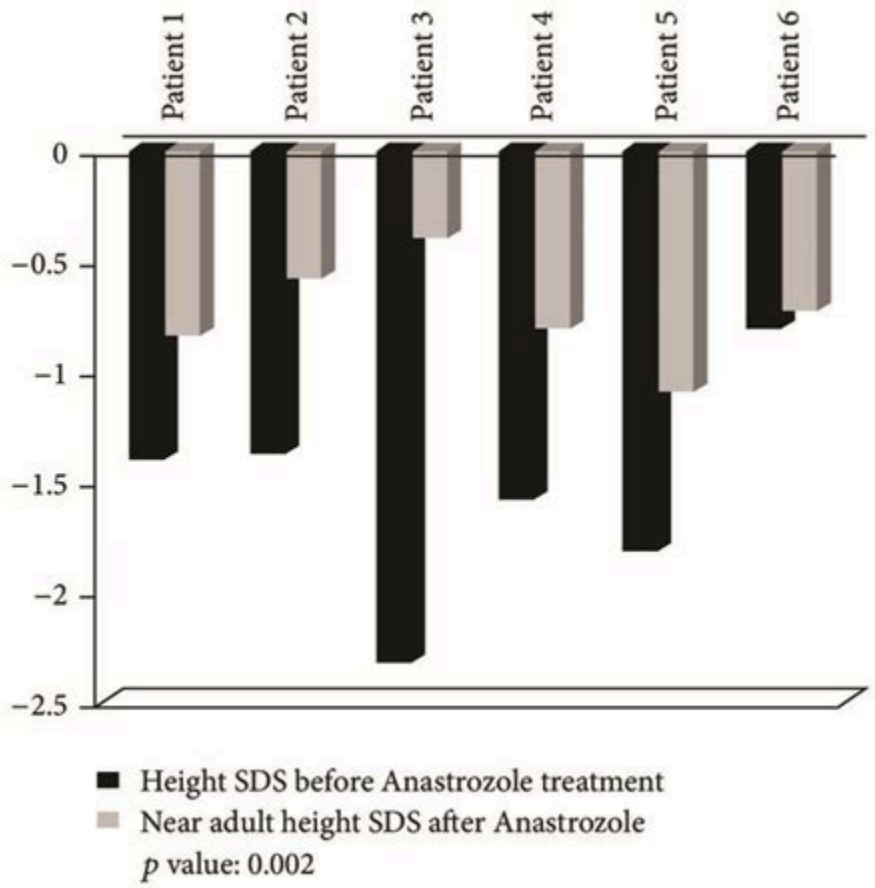
April 4, 2016 Source: Endocrine Society Summary: Aromatase inhibitors, when used for up to three years in combination with growth hormone, may effectively and safely help very short adolescent.

Letrozole Significantly Improves Growth Potential in a Pubertal Boy .



When given during the course of puberty, anastrozole (A), an aromatase inhibitor, has been shown to increase the predicted adult height (PAH) of GH-deficient (GHD) boys treated with recombinant human growth hormone (rhGH).

The Efficacy of Anastrozole and Growth Hormone Therapy on . - Hindawi



Conclusions: Anastrozole increases adult height potential of adolescent boys on GH therapy while maintaining normal pubertal progression after 2-3 yr. This treatment offers an alternative in promoting growth in GH-deficient boys in puberty. Long-term follow up is needed to elucidate fully the safety and efficacy of this approach.

Should Skeletal Maturation Be Manipulated for Extra Height Gain?

frontiers in Endocrinology

REVIEW
published: 16 December 2021
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Should Skeletal Maturation Be Manipulated for Extra Height Gain?

*Jan M. Wit**

Division of Pediatric Endocrinology, Department of Pediatrics, Willem-Alexander Children's Hospital, Leiden University Medical Center, Leiden, Netherlands

Skeletal maturation can be delayed by reducing the exposure to estrogens, either by halting pubertal development through administering a GnRH analogue (GnRHa), or by blocking the conversion of androgens to estrogens through an aromatase inhibitor (AI). These agents have been investigated in children with growth disorders (off-label), either alone or in combination with recombinant human growth hormone (rhGH). GnRHa is effective in attaining a normal adult height (AH) in the treatment of children with central precocious puberty, but its effect in short children with normal timing of puberty is equivocal. If rhGH-treated children with growth hormone deficiency or those who were born small-for-gestational age are still short at pubertal onset, co-treatment with a GnRHa for 2-3 years increases AH. A similar effect was seen by adding rhGH to GnRHa treatment of children with central precocious puberty with a poor AH prediction and by adding rhGH plus GnRHa to children with congenital adrenal hyperplasia with a poor predicted adult height on conventional treatment with gluco- and mineralocorticoids. In girls with idiopathic short stature and relatively early puberty, rhGH plus GnRHa increases AH. Administration of letrozole to boys with constitutional delay of growth puberty may increase AH, and rhGH plus anastrozole may increase AH in boys with growth hormone deficiency or idiopathic short stature, but the lack of data on attained AH and potential selective loss-of-follow-up in several studies precludes firm conclusions. GnRHas appear to have a good overall safety profile, while for aromatase inhibitors conflicting data have been reported.

Keywords: growth, skeletal maturation, bone age, adult height, aromatase inhibitors, GnRH analogue, growth hormone, predicted adult height

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1 INTRODUCTION

There are three therapeutic approaches to increase adult height (AH) for a child with a growth disorder. First, recombinant human growth hormone (rhGH) has been approved for several causes of short stature in children, and in most conditions this treatment (if initiated at a young age) results in an AH within the genetic target height range of the patient. Second, experiments of nature have suggested that keeping the estrogen exposure low in adolescence might delay skeletal maturation and increase AH, which has led to clinical studies on the efficacy and safety of two forms of medication aimed at reducing estrogen exposure, i.e. gonadotropin-releasing hormone (GnRH) analogues (GnRHas) and aromatase inhibitors (AIs). Third, also the combination of rhGH and a GnRHa or AI has been investigated,

Abstract. Aromatase inhibitors (AIs) are a class of drugs that prevent conversion of androgens to estrogens, and that are approved in the United States as adjunctive treatment of estrogen receptor-positive breast cancer. Because ultimate fusion of the growth plates is estrogen-dependent in both boys and girls, AI administration may help to slow .

Anastrozole Increases Predicted Adult Height of Short Adolescent Males .

ORIGINAL ARTICLE

Endocrine Care

Anastrozole Increases Predicted Adult Height of Short Adolescent Males Treated with Growth Hormone: A Randomized, Placebo-Controlled, Multicenter Trial for One to Three Years

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Context: The process of epiphyseal fusion during puberty is regulated by estrogen, even in males.

Objective: Our objective was to investigate whether anastrozole, a potent aromatase inhibitor, could delay bone age acceleration and increase predicted adult height in adolescent boys with GH deficiency.

Methods: Fifty-two adolescent males with GH deficiency treated with GH were randomized to cotreatment with anastrozole or placebo daily for up to 36 months.

Results: Fifty subjects completed 12 months, 41 completed 24 months, and 28 completed 36 months. Linear growth was comparable between groups; however, there was a significantly slower increase in bone age advancement from baseline in the anastrozole group *vs.* placebo group after 2 yr (+1.8 ± 0.1 *vs.* +2.7 ± 0.1 yr, $P < 0.0001$) and after 3 yr (+2.5 ± 0.2 *vs.* +4.1 ± 0.1 yr, $P < 0.0001$). This resulted in a net increase in predicted adult height of +4.5 ± 1.2 cm in the anastrozole group at 24 months and +6.7 ± 1.4 cm at 36 months as compared with a 1-cm gain at both time points in the placebo group. Estradiol and estrone concentrations increased less in the anastrozole group compared with placebo group. All boys on the aromatase inhibitor had normal tempo of virilization. Safety data, including glucose, and plasma lipid concentrations were comparable between groups.

Conclusions: Anastrozole increases adult height potential of adolescent boys on GH therapy while maintaining normal pubertal progression after 2–3 yr. This treatment offers an alternative in promoting growth in GH-deficient boys in puberty. Long-term follow up is needed to elucidate fully the safety and efficacy of this approach. (*J Clin Endocrinol Metab* 93: 823–831, 2008)

A number of strategies have evolved to increase height potential in GH-deficient children who are in puberty, such as using high-dose GH therapy (1) or GnRH analogs in addition to GH (2–5). The latter strategy has also been used in non-GH-deficient children, with mixed results (6–8). The consequences of gonadal suppression regarding bone accretion/bone density and the psychological impact of suppressing physiological puberty in an already short child have not been fully studied to date.

Studies of male patients with mutations in the estrogen receptor gene (9) or in the aromatase enzyme gene (10, 11) as well

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Abbreviations: BMD, Bone mineral density; DXA, dual-energy x-ray absorptiometry; LC-MS/MS, liquid chromatography-tandem mass spectrometry; SDS, SD score.

These studies all show that treatment with the aromatase inhibitors letrozole and anastrozole effectively delays bone maturation and increases predicted adult height in boys with constitutional delay of growth and puberty (CDGP), idiopathic short stature and growth hormone deficiency.

- https://sites.google.com/view/aasreview/test-enanthate-250-mg-cycle
- https://groups.google.com/g/ripped-reckoners/c/F664zhGg1ro
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